

Serial No. 10/088,400

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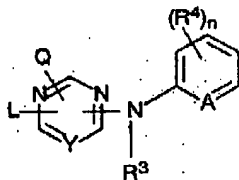
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## APPENDIX II:

CLAIM AMENDMENTS

Enter new Claims 26 as indicated in the following listing of the claims:

1. (previously presented) Rate-controlled release particles, comprising, in a polymer matrix consisting of a homo- or copolymer of N-vinylpyrrolidone, an active ingredient as a solid dispersion in the polymeric matrix and from 5 to 25% b.w. of hydroxypropyl methyl cellulose, and optionally further comprising a surfactant, and wherein the active ingredient is a compound of formula I



a N-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric form thereof, wherein

Y is CR<sup>5</sup> or N;

A is CH, CR<sup>4</sup> or N;

n is 0, 1, 2, 3 or 4;

Q is -NR<sup>1</sup>R<sup>2</sup> or when Y is CR<sup>5</sup> then Q may also be hydrogen;

R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, hydroxy, C<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkyloxy, C<sub>1-12</sub>alkylcarbonyl, C<sub>1-12</sub>alkyloxycarbonyl, aryl, amino, mono- or di(C<sub>1-12</sub>alkyl)amino, mono- or di(C<sub>1-12</sub>alkyl)aminocarbonyl

wherein each of the aforementioned C<sub>1-12</sub>alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C<sub>1-6</sub>alkyloxy, hydroxy-C<sub>1-6</sub>alkyloxy, carboxyl, C<sub>1-6</sub>alkyloxycarbonyl, cyano, amino, imido, aminocarbonyl, aminocarbonylamino, mono- or di(C<sub>1-6</sub>alkyl)amino, aryl and Het; or

R<sup>1</sup> and R<sup>2</sup> taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C<sub>1-12</sub>alkyl)aminoC<sub>1-4</sub>-alkylidene;

R<sup>3</sup> is hydrogen, aryl, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxycarbonyl, C<sub>1-6</sub>alkyl substituted with C<sub>1-6</sub>alkyloxycarbonyl; and

each R<sup>4</sup> independently is hydroxy, halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalome-

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thyloxy, or when Y is CR<sup>5</sup> then R<sup>4</sup> may also represent C<sub>1-6</sub>alkyl substituted with cyano or amino carbonyl;

R<sup>5</sup> is hydrogen or C<sub>1-4</sub>alkyl;

L is -X<sup>1</sup>-R<sup>6</sup> or -X<sup>2</sup>-Alk-R<sup>7</sup> wherein

R<sup>6</sup> and R<sup>7</sup> each independently are phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyloxy carbonyl, formyl, cyano, nitro, amino, and trifluoromethyl; or when Y is CR<sup>5</sup> then R<sup>6</sup> and R<sup>7</sup> may also be selected from phenyl substituted with one, two, three, four or five substituents each independently selected from aminocarbonyl, trihalomethyloxy and trihalomethyl; or when Y is N then R<sup>6</sup> and R<sup>7</sup> may also be selected from indanyl or indolyl, each of said indanyl or indolyl may be substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyloxy carbonyl, formyl, cyano, nitro, amino, and trifluoromethyl;

X<sup>1</sup> and X<sup>2</sup> are each independently -NR<sup>3</sup>-, -NH-NH-, -N=N-, -O-, -S-, -S(=O)- or -S(=O)<sub>2</sub>-;

Alk is C<sub>1-4</sub>alkanediyl; or

when Y is CR<sup>5</sup> then L may also be selected from C<sub>1-10</sub>alkyl, C<sub>3-10</sub>alkenyl, C<sub>3-10</sub>alkynyl, C<sub>3-7</sub>cycloalkyl, or C<sub>1-10</sub>alkyl substituted with one or two substituents independently selected from C<sub>3-7</sub>cycloalkyl, indanyl, indolyl and phenyl, wherein said phenyl, indanyl and indolyl may be substituted with one, two, three, four or where possible five substituents each independently selected from halo, hydroxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, cyano, aminocarbonyl, C<sub>1-6</sub>alkyloxy carbonyl, formyl, nitro, amino, trihalomethyl, trihalomethyloxy and C<sub>1-6</sub>alkylcarbonyl;

aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, cyano, nitro and trifluoromethyl;

Het is an aliphatic or aromatic heterocyclic radical; said aliphatic heterocyclic radical is selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, tetrahydrofuranlyl and tetrahydrothienyl

wherein each of said aliphatic heterocyclic radical may optionally be substituted with an oxo group; and said aromatic

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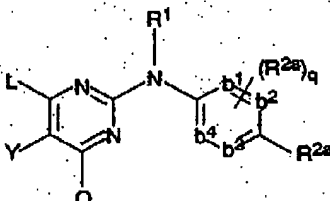
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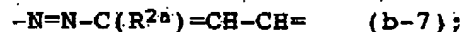
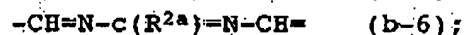
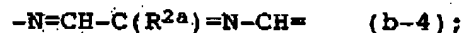
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heterocyclic radical is selected from pyrrolyl, furanyl, thienyl, pyridyl, pyrimidinyl, pyrazinyl and pyridazinyl wherein each of said aromatic heterocyclic radical may optionally be substituted with hydroxy, or a compound of formula II



the N-oxides, the pharmaceutically acceptable addition salts, quaternary amines and the stereochemically isomeric forms thereof, wherein

$-b^1-b^2-C(R^{2a})=b^3-b^4-$  represents a bivalent radical of formula



q is 0, 1, 2; or where possible q is 3 or 4;

R<sup>1</sup> is hydrogen, aryl, formyl, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxycarbonyl, C<sub>1-6</sub>alkyl substituted with formyl, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyloxycarbonyl;

R<sup>2a</sup> is cyano, aminocarbonyl, mono- or di(methyl)aminocarbonyl, C<sub>1-6</sub>alkyl substituted with cyano, aminocarbonyl or mono- or di(methyl)aminocarbonyl, C<sub>2-6</sub>alkenyl substituted with cyano, or C<sub>2-6</sub>alkynyl substituted with cyano;

each R<sup>2</sup> independently is hydroxy, halo, C<sub>1-6</sub>alkyl optionally substituted with cyano or  $-C(=O)R^6$ , C<sub>3-7</sub>cycloalkyl, C<sub>2-6</sub>alkenyl optionally substituted with one or more halogen atoms or cyano, C<sub>2-6</sub>alkynyl optionally substituted with one or more halogen atoms or cyano, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio,  $-S(=O)OR^6$ ,  $-NH-S(=O)R^6$ ,  $-C(=O)R^6$ ,  $-NEC(=O)H$ ,  $-C(=O)NHNH_2$ ,  $-NEC(=O)R^6$ ,  $-C(=NH)R^6$  or a radical of formula

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(c)

wherein each A independently is N, CH or CR<sup>6</sup>;

B is NH, O, S or NR<sup>6</sup>;

p is 1 or 2; and

R<sup>6</sup> is methyl, amino, mono- or dimethylamino or polyhalomethyl;

L is C<sub>1-10</sub>alkyl, C<sub>2-10</sub>alkenyl, C<sub>2-10</sub>alkynyl, C<sub>3-7</sub>cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from

\* C<sub>3-7</sub>cycloalkyl,

\* indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethyloxy and C<sub>1-6</sub>alkylcarbonyl,

\* phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R<sup>2</sup>; or

L is -X-R<sup>3</sup> wherein

R<sup>3</sup> is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R<sup>2</sup>; and

X is -NH<sup>1</sup>-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)- or -S(=O)<sub>2</sub>-;

Q represents hydrogen, C<sub>1-6</sub>alkyl, halo, polyhaloC<sub>1-6</sub>alkyl or -NR<sup>4</sup>R<sup>5</sup>; and

R<sup>4</sup> and R<sup>5</sup> are each independently selected from hydrogen, hydroxy, C<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkyloxy, C<sub>1-12</sub>alkylcarbonyl, C<sub>1-12</sub>alkyloxycarbonyl, aryl, amino, mono- or di(C<sub>1-12</sub>alkyl)amino, mono- or di(C<sub>1-12</sub>alkyl)aminocarbonyl

wherein each of the aforementioned C<sub>1-12</sub>alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C<sub>1-6</sub>al-

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kyloxy, hydroxyc<sub>1-6</sub>alkyloxy, carboxyl, C<sub>1-6</sub>alkyloxy-carbonyl, cyano, amino, imino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(O)<sub>p</sub>R<sup>6</sup>, -NH-S(=O)<sub>p</sub>R<sup>6</sup>, -C(=O)R<sup>6</sup>, -NHC(=O)H, -C(=O)NHNH<sub>2</sub>, -NHC(O)R<sup>6</sup>, -C(=NH)R<sup>6</sup>, aryl and Het; or

R<sup>4</sup> and R<sup>5</sup> taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C<sub>1-12</sub>alkyl)aminoC<sub>1-4</sub>-alkylidene;

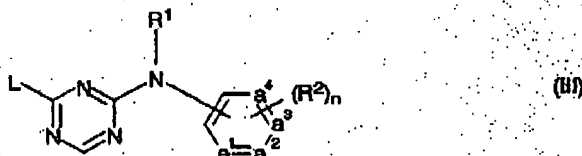
Y represents hydroxy, halo, C<sub>3-7</sub>cycloalkyl, C<sub>2-6</sub>alkenyl optionally substituted with one or more halogen atoms, C<sub>2-6</sub>alkynyl optionally substituted with one or more halogen atoms, C<sub>1-6</sub>alkyl substituted with cyano or -C(=O)R<sup>6</sup>, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkyloxy-carbonyl, carboxyl, cyano, nitro, amino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)<sub>p</sub>R<sup>6</sup>, -NH-S(=O)<sub>p</sub>R<sup>6</sup>, -C(=O)R<sup>6</sup>, -NHC(=O)H, -C(=O)NHNH<sub>2</sub>, -NHC(=O)R<sup>6</sup>, -C(NH)R<sup>6</sup> or aryl;

aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>1-6</sub>alkyloxy, cyano, nitro, polyhaloC<sub>1-6</sub>alkyl and polyhaloC<sub>1-6</sub>alkyloxy;

Het is an aliphatic or aromatic heterocyclic radical;

said aliphatic heterocyclic radical is selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, tetrahydrofuranyl and tetrahydrothienyl wherein each of said aliphatic heterocyclic radical may optionally be substituted with an oxo group; and said aromatic heterocyclic radical is selected from pyrrolyl, furanyl, thienyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl wherein each of said aromatic heterocyclic radical may optionally be substituted with hydroxy,

or a compound of formula III



a N-oxide, a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof, wherein -a<sup>1</sup>=a<sup>2</sup>-a<sup>3</sup>=a<sup>4</sup>- represents a bivalent radical of formula



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$$-N=CH-CH=CH- \quad (a-2);$$

$$-N=CH-N=CH- \quad (a-3);$$

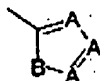
$$-N=CH-CH=N- \quad (a-4);$$

$$-N=N-CH=CH- \quad (a-5);$$

n is 0, 1, 2, 3 or 4; and in case  $-a^1=a^2=a^3=a^4-$  is (a-1), then n may also be 5;

R<sup>1</sup> is hydrogen, aryl, formyl, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxycarbonyl, C<sub>1-6</sub>alkyl substituted with formyl, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyloxycarbonyl; and

each R<sup>2</sup> independently is hydroxy, halo, C<sub>1-6</sub>alkyl optionally substituted with cyano or  $-C(=O)R^4$ , C<sub>3-7</sub>cycloalkyl, C<sub>2-6</sub>alkenyl optionally substituted with one or more halogen atoms or cyano, C<sub>2-6</sub>alkynyl optionally substituted with one or more halogen atoms or cyano, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio,  $-S(=O)_pR^4$ ,  $-NH-S(=O)_pR^4$ ,  $-C(=O)R^4$ ,  $-NHC(=O)R$ ,  $-C(=O)NHNH_2$ ,  $NHC(=O)R^4$ ,  $-C(=NH)R^4$  or a radical of formula



(c)

wherein each A independently is N, CH or CR<sup>4</sup>;

B is NH, O, S or NR<sup>4</sup>;

p is 1 or 2; and

R<sup>4</sup> is methyl, amino, mono- or dimethylamino or polyhalomethyl;

L is C<sub>4-10</sub>alkyl, C<sub>2-10</sub>alkenyl, C<sub>2-10</sub>alkynyl, C<sub>3-7</sub>cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from

\* C<sub>3-7</sub>cycloalkyl,

\* indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethyloxy and C<sub>1-6</sub>alkylcarbonyl,

\* phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents

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each independently selected from the substituents defined in R<sup>2</sup>; or

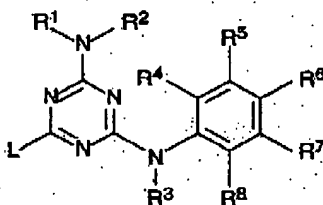
L is -X-R<sup>3</sup> wherein

R<sup>3</sup> is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with two, three, four or five substituents each independently selected from the substituents defined in R<sup>2</sup>; and

X is -NR<sup>1</sup>-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)- or -S(=O)<sub>2</sub>-;

aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>1-6</sub>alkyloxy, cyano, nitro, polyhaloC<sub>1-6</sub>alkyl and polyhaloC<sub>1-6</sub>alkyloxy,

or a compound of formula IV



(IV)

the pharmaceutically acceptable acid addition salts and the stereochemically isomeric forms thereof, wherein

R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen; hydroxy; amino; C<sub>1-6</sub>alkyl; C<sub>1-6</sub>alkyloxy; C<sub>1-6</sub>alkylcarbonyl; C<sub>1-6</sub>alkyloxy-carbonyl; Ar<sup>1</sup>; mono- or di(C<sub>1-6</sub>alkyl)amino; mono- or di(C<sub>1-6</sub>alkyl)aminocarbonyl; dihydro-2(3H)-furanone; C<sub>1-6</sub>alkyl substituted with one or two substituents each independently selected from amino, imino, aminocarbonyl, aminocarbonylamino, hydroxy, hydroxyc<sub>1-6</sub>alkyloxy, carboxyl, mono- or di(C<sub>1-6</sub>alkyl)amino, C<sub>1-6</sub>alkyloxy-carbonyl and thienyl; or

R<sup>1</sup> and R<sup>2</sup> taken together may form pyrrolidinyl, piperidinyl, morpholinyl, azido or mono- or di(C<sub>1-6</sub>alkyl)aminoC<sub>1-4</sub>-alkylidene;

R<sup>3</sup> is hydrogen, Ar<sup>1</sup>, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy-carbonyl, C<sub>1-6</sub>alkyl substituted with C<sub>1-6</sub>alkyloxy-carbonyl; and

R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> are each independently selected from hydrogen; hydroxy, halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl or trihalomethyloxy;

L is C<sub>1-10</sub>alkyl, C<sub>3-10</sub>alkenyl; C<sub>3-10</sub>alkynyl; C<sub>3-7</sub>cycloalkyl, or

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L is C<sub>1-10</sub>alkyl substituted with one or two substituents independently selected from C<sub>3-7</sub>cycloalkyl;

indolyl or indolyl substituted with one, two, three or four substituents each independently selected from halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C<sub>1-6</sub>alkylcarbonyl;

phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, cyano, aminocarbonyl, nitro, amino, trihalomethyl, trihalomethyloxy, C<sub>1-6</sub>alkylcarbonyl; and,

Ar<sup>1</sup> is phenyl, or phenyl substituted with one, two or three substituents each independently selected from halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, cyano, nitro or trifluoromethyl;

with the proviso that compounds (a) to (o)

Co. No.	Alk	R <sup>1</sup> /R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>	R <sup>6</sup>	R <sup>7</sup>	R <sup>8</sup>
a	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	CH <sub>3</sub>	H	H	H	H
b	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	NO <sub>2</sub>	H	H
c	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	C <sub>6</sub> H <sub>5</sub>	H	H	H	H	H
d	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	NO <sub>2</sub>	H	CH <sub>3</sub>	H	H
e	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	NH <sub>2</sub>	H	H
f	4-(2-methylpropyl)phenylmethyl	H/H	H	H	CF <sub>3</sub>	H	H	H
g	1-(4-(2-methylpropyl)phenyl)ethyl	H/H	H	H	H	Cl	H	H
h	4-(2-methylpropyl)phenylmethyl	H/H	H	H	H	H	H	H
i	3,4-dimethoxyphenylmethyl	H/H	H	H	H	H	H	H
j	2,3-dimethoxyphenylmethyl	H/H	H	H	H	H	H	H
k	3,4-diethoxyphenylmethyl	H/H	H	H	H	H	H	H
l	2-(3,5-(1,1-dimethylethyl)-4-hydroxy-phenyl)ethyl	H/H	H	H	H	H	H	H
m	2-(3,5-(1,1-dimethylethyl)-4-hydroxy-phenyl)ethyl	H/H	H	H	t-Bu	OH	t-Bu	H
n	Phenylmethyl	H/H	H	CH <sub>3</sub>	H	H	H	H
o	Phenylmethyl	H/H	H	H	H	H	H	H

are not included,

or a compound of formula v

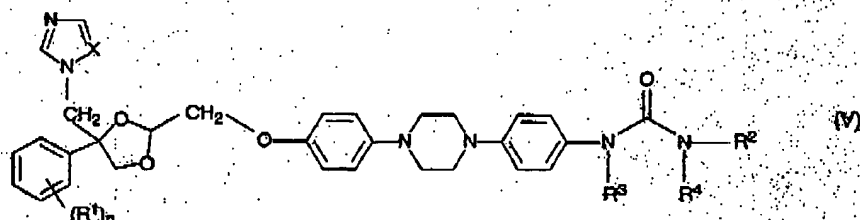
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the *N*-oxide forms, the pharmaceutically acceptable acid addition salts and stereochemically isomeric forms thereof,

wherein

*n* is zero, 1, 2 or 3;

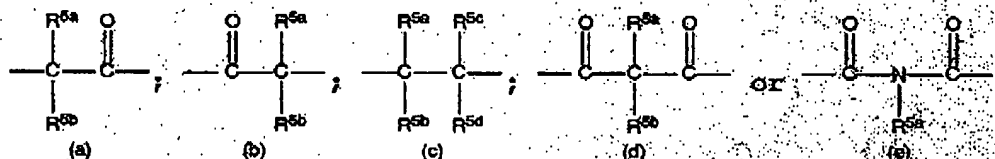
*X* is N or CH;

each *R*<sup>1</sup> independently is halo, nitro, cyano, amino, hydroxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy or trifluoromethyl;

*R*<sup>2</sup> is hydrogen; C<sub>3-7</sub>alkenyl; C<sub>3-7</sub>alkynyl, aryl; C<sub>3-7</sub>cycloalkyl; C<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkyl substituted with hydroxy, C<sub>1-4</sub>alkyloxy, C<sub>3-7</sub>cycloalkyl or aryl;

*R*<sup>3</sup> and *R*<sup>4</sup> each independently are hydrogen, C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl or aryl; or

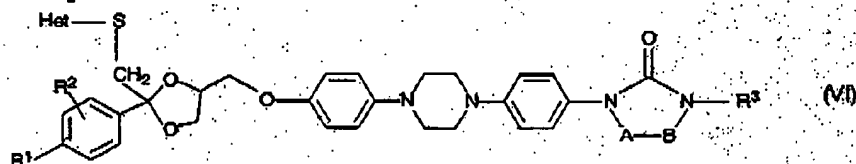
*R*<sup>3</sup> and *R*<sup>4</sup> taken together form a bivalent radical -*R*<sup>3</sup>-*R*<sup>4</sup>- of formula:



wherein *R*<sup>5a</sup>, *R*<sup>5b</sup>, *R*<sup>5c</sup>, *R*<sup>5d</sup> each independently are hydrogen, C<sub>1-6</sub>alkyl or aryl; and

aryl is phenyl or phenyl substituted with one, two or three substituents selected from halo, nitro, cyano, amino, hydroxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy or trifluoromethyl,

or a compound of formula VI



the *N*-oxides, the stereochemically isomeric forms thereof, and the pharmaceutically acceptable acid addition salts, wherein A and B taken together form a bivalent radical of formula:

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- N=CH- (a),
- CH=N- (b),
- CH<sub>2</sub>-CH<sub>2</sub>- (c),
- CH=CH- (d),
- C(=O)-CH<sub>2</sub>- (e),
- CH<sub>2</sub>-C(=O)- (f),

in the bivalent radicals- of formula (a) and (h) the hydrogen atom may be replaced by C<sub>1-6</sub>alkyl; in the bivalent radicals of formula (c), (d), (e), (f), one or two hydrogen atoms may be replaced by C<sub>1-6</sub>alkyl;

R<sup>1</sup> is hydrogen, C<sub>1-6</sub>alkyl or halo;

R<sup>2</sup> is hydrogen or halo;

R<sup>3</sup> is hydrogen; C<sub>1-8</sub>alkyl; C<sub>3-6</sub>cycloalkyl; or C<sub>1-8</sub>alkyl substituted with hydroxy, oxo, C<sub>3-6</sub>cycloalkyl or aryl;

Het is a heterocycle selected from the group consisting of pyridine; pyridine substituted with one or two substituents selected from C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, trihalomethyl, amino, mono- or di(C<sub>1-6</sub>alkyl)amino or aryl;

pyrimidine; pyrimidine substituted with one or two substituents selected from C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, trihalomethyl, amino, mono- or di(C<sub>1-6</sub>alkyl)-amino or aryl;

tetrazole; tetrazole substituted with C<sub>1-6</sub>alkyl or aryl;

triazole; triazole substituted with one or two substituents selected from C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, trihalomethyl, amino, mono- or di(C<sub>1-6</sub>alkyl)-amino;

thiadiazole; thiadiazole substituted with one or two substituents selected from C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, trihalomethyl, amino, mono- or di(C<sub>1-6</sub>alkyl)-amino;

oxadiazole substituted with one or two substituents selected from C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, trihalomethyl, amino, mono- or di(C<sub>1-6</sub>alkyl)amino;

imidazole; imidazole substituted with one or two substituents selected from C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, trihalomethyl, amino, mono- or di(C<sub>1-6</sub>alkyl)amino;

thiazole; thiazole substituted with one or two substituents selected from C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, trihalomethyl, amino, mono- or di(C<sub>1-6</sub>alkyl)amino;

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oxazole; oxazole substituted with one or two substituents selected from C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, trihalomethyl, amino, mono- or di(C<sub>1-6</sub>alkyl)amino;

aryl is phenyl or phenyl substituted with C<sub>1-6</sub>alkyl or halo, and the heterocyclic radical "Het" is bound to the sulfur atom via a carbon atom.

2. (original) Particles according to claim 1, wherein the copolymer of N-vinylpyrrolidone is a copolymer with vinyl acetate.
4. (previously presented) Particles according to claim 1, which comprise a surfactant and wherein the surfactant is a PEG-n-hydrogenated castor oil, or a low molecular weight polyoxyethylene polyoxypropylene block copolymer.
6. (previously presented) Particles according to claim 1, further comprising citric acid in amounts of up to 5% b.w.
7. (previously presented) Particles according to claim 1, wherein the homo- or copolymer of N-vinylpyrrolidone is used in amounts of from 40 to 70% b.w. of the total weight of the dosage form.
8. (original) Particles according to claim 7, wherein the homo- or copolymer of N-vinylpyrrolidone is used in amounts of from 50 to 65 % b.w..
10. (previously presented) Particles according to claim 1, wherein the controlled release is a sustained release.
11. (previously presented) Particles according to claim 10, comprising the hydroxypropyl methyl cellulose in amounts of from 5 to 10 % b.w..
12. (previously presented) Particles according to claim 1, obtained by forming a homogeneous mixture of the components in the form of a melt, extruding said mixture and shaping of the extrudate.
13. (previously presented) Particles according to claim 1, comprising a compound selected from the group consisting of  
4-[[4-[(2,4,6-trimethylphenyl)amino]-2-pyrimidinyl]amino]benzonitrile;  
4-[[2-[(cyanophenyl)amino]-4-pyrimidinyl]amino]-3,5-dimethylbenzonitrile;  
4-[[4-amino-5-chloro-6-[(2,4,6-trimethylphenyl)amino]-2-pyrimidinyl]-amino]benzonitrile;

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4-[[5-chloro-4-[(2,4,6-trimethylphenyl)amino]-2-pyrimidinyl]amino]benzonitrile;

4-[[5-bromo-4-(4-cyano-2,6-dimethylphenoxy)-2-pyrimidin]amino]benzonitrile;

4-[[4-amino-5-chloro-6-[(4-cyano-2,6-dimethylphenyl)amino]-2-pyrimidinyl]amino]benzonitrile;

4-[[5-bromo-6-[(4-cyano-2,6-dimethylphenyl)amino]-2-pyrimidinyl]amino]benzonitrile;

4-[[4-amino-5-chloro-6-[(4-cyano-2,6-dimethylphenoxy)-2-pyrimidinyl]amino]benzonitrile;

4-[[4-amino-5-bromo-6-(4-cyano-2,6-dimethylphenoxy)-2-pyrimidinyl]amino]benzonitrile;

4-[[4-[(2,4,6-trimethylphenyl)amino]-1,3,5-triazin-2-yl]amino]benzonitrile;

4-[[4-amino-6-[(2,6-dichlorophenyl)methyl]-1,3,5-triazin-2-yl]amino]benzonitrile;

4-[[4-[(2,6-dichlorophenyl)methyl]-6-(hydroxyamino)-1,3,5-triazin-2-yl]amino]benzonitrile;

1-[4-[4-[4-[(2,4-difluorophenyl)-4-(1H-1,2,4-triazol-1-yl)methyl]-1,3-dioxolan-2-yl]methoxy]phenyl]-1-piperazinyl]-phenyl]-3-(1-methylethyl)-2-imidazolidinone;

(-)-[2S-[2alpha, 4alpha(S\*)]]-4-[4-[4-[4-[[2-(4-chlorophenyl)-2-[(4-methyl-4H-1,2,4-triazol-3-yl)thio]methyl]-1,3-dioxolan-4-yl]methoxyl]phenyl]-1-piperazinyl]phenyl]-2,4-dihydro-2-(1-methyl-propyl)-3H-1,2,4-triazol-3-one,

a N-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric form thereof.

14. (previously presented) Pharmaceutical dosage form, comprising particles according to a claim 1.
15. (previously presented) Pharmaceutical dosage forms according to claim 14, further comprising one or more pharmaceutically acceptable excipients.
16. (previously presented) Particles according to claim 4, which meet one or both of the following requirements:
  - the surfactant has a HLB-value of from 10 to 18;
  - the surfactant is present in the particles in an amount of from 5 to 20% by weight.

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20. (previously presented) Particles according to claim 1, consisting essentially of the active ingredient,  
from 40 to 70% by weight of the a homo- or copolymer of N-vinylpyrrolidone,  
from 5 to 20% by weight of the surfactant,  
up to 5% by weight of citric acid, and  
from 5 to 25% by weight of hydroxypropyl methyl cellulose.
21. (previously presented) Particles according to claim 20, wherein the surfactant has a HLB-value of from 10 to 18.
22. (previously presented) Particles according to claim 21, wherein the surfactant is a PEG-n-hydrogenated castor oil and/or a low molecular weight polyoxyethylene polyoxypropylene block copolymer.
23. (previously presented) Particles according to claim 1, obtained by a process comprising forming a homogeneous mixture of the components in the form of a melt, extruding said melt and shaping the obtained extrudate.
24. (previously presented) Particles according to claim 16, obtained by a process comprising forming a homogeneous mixture of the components in the form of a melt, extruding said melt and shaping the obtained extrudate.
25. (previously presented) Particles according to claim 20, obtained by a process comprising forming a homogeneous mixture of the components in the form of a melt, extruding said melt and shaping the obtained extrudate.
26. (new) Particles according to claim 1, wherein the homo- or copolymer of N-vinylpyrrolidone has a Fikentscher K value of from 17 to 90.

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